REMARKS

The specification has been amended to capitalize HERCEPTIN™ and provide the generic name where necessary.

Claim 1 has been revised to include a re-phrasing of the preamble and to recite "detecting in an analyte sample" which is supported at least on pages 19-20, paragraph [0037], of the instant application. The instant application further describes "analyte sample" in terms understood to the skilled person in paragraph [0029]. Claim 1 has also been revised to include description of the inherent effects of interaction between the substance and the receptor, which is supported at least at paragraph [0024] of the instant application.

Otherwise, the claim has been revised to use alternative language to encompass the same intended subject matter.

Claim 10 has been revised to remove the recitation of "HERCEPTIN™" without altering the scope of the claim as encompassed by the term "trastuzumab."

Claim 12 has been revised to feature components of a reagent kit. Support for the amendment is found in the instant application on at least pages 17-18 in paragraphs [0033] and [0034] as well as paragraph [0035] with respect to antibodies.

No new matter has been introduced, and entry of the new and revised claims and specification are respectfully requested.

Objections to the Specification

The specification has been amended to capitalize the trademark HERCEPTIN™ and to provide the generic name where previously omitted in Table 1. Applicants respectfully submit that the objections to the specification are overcome by the above revisions to the specification. Reconsideration and withdrawal of the objections is requested.

Alleged Rejection Under 35 U.S.C. §101

Claims 1-20 were rejected under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter. Claim 1 has been revised to feature acts of detecting in an analyte sample the expression of discrete and recognized genes and/or polypeptides (receptor and substances that interact with the receptor on the surface of and/or within the cell membrane). Applicants

respectfully submit that this amendment overcomes the rejection, and reconsideration and withdrawal of the rejection thereof are respectfully requested.

Alleged Rejection Under 35 U.S.C. §112

Claims 1-3, 5, 6, 8, 9, and 11-20 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to be supported by an enabling disclosure. Applicants have carefully reviewed the statement of the rejection and respectfully traverse because no *prima facie* case of a lack of enablement has been presented. Reconsideration is respectfully requested based on the following.

Based on the statement of the rejection, Applicants believe that the rejection is based on the assertion that the unpredictability of determining patient outcome when administered an anticancer drug based on expression of specific genes is well known in the art. In support of this assertion, the rejection cites Pasche et al. (Best practice research: Clinical Gastroenterology Vol. 16(2) pp. 331-345, April 2002) and Ross et al. (Seminars in Cancer Biology, Vol. 9(2), pp. 125-138, April 1999). The Examiner also cites Price-Schiavi et al. (Int. J. Cancer Vol. 99, pp. 783-791, 2002) for findings that, as asserted, are not consistent with the findings in the current application.

Applicants respectfully point out that the skilled artisan is well acquainted with detecting in an analyte sample the gene and/or the expressed product of a receptor. Similarly, the skilled person is familiar with the detecting in an analyte sample the gene and/or the expressed product of a substance that interacts with the receptor on the surface of and/or within the cell membrane.

Given this knowledge and understanding, it is wholly within the abilities of the skilled person to select a receptor, and a substance that interacts with it on the surface of or within the cell membrane, and to detect them in an analyte sample, such as a tissue sample. Stated differently, there is no objective reason (or direct evidence) to doubt that a skilled person would easily be able to examine the expression of both a receptor and a substance (or ligand) that interacts with the receptor on the surface of and/or within the cell membrane. None of the cited documents indicate otherwise.

Additionally, this level of skill in the relevant field provides the necessary direction or guidance, even if relevant working examples are not provided. Moreover, this level of knowledge and experience in the field limits the amount of necessary experimentation to no

more than that which is routine and repetitive. This minimal amount of experimentation is the very opposite of "undue experimentation" which is necessary to support a *prima facie* case of non-enablement.

The documents cited by the Examiner do not support a *prima facie* case of non-enablement. It is asserted that Pasche et al. discuss the discrepancies of her-2/neu expression in colorectal cancer patients and its significance to prognosis and that the discrepancies do not currently support its use in the management of patients with colorectal cancer, and that Ross et al. report that three studies found that elevated serum HER-2 neu protein predicted therapy resistance, whereas three studies did not demonstrate this association. Neither of these documents, however, report detection in combination with a ligand that interacts with HER-2 to affect its expression or function as featured in the claims. Moreover, none of these documents describe a mucin glycoprotein, such as MUC4, as featured in the pending claims.

With respect to the Price-Schiavi et al. document, that reference reports A375 cells (human melanoma cells) and MCF7 cells (human breast adenocarcinoma cells) which are transfected to **overexpress a rat** MUC4/sialomucin complex. Without overexpression of MUC4/sialomucin, the human tumor cells used by the authors do not express MUC4/sialomucin at all (see Price-Schiavi, Figures 2A and 5A). Therefore, these cells do not have an intracellular system of regulating HER2 (erbB-2) expression and activity as would be found in a human cancer cell that expresses **human** MUC4. So it is uncertain whether the effects of phosphorylation via binding of HER2 with antibody in these cells functions in the same manner as a human cell that expresses a HER2 ligand.

A similar effect was shown in rats (see Price-Schiavi et al., last paragraph, column 2, page 783). Rat cells were made to overexpress MUC4/sialomucin at a 10,000-fold higher than the level in a normal virgin gland. One of skill in the art would recognize that the overexpression levels in this reference is not necessarily reflective of cells not transfected to overexpress MUC4/sialomucin at such a high level. So the results provide no reasonable expectation that cells expressing the complex at lower levels will show a similar effect. As a result, the Price-Schiavi et al. document does not negate the presence of enablement for the invention as claimed.

In light of the foregoing, Applicants submit that this rejection is misplaced and may be properly withdrawn.

Alleged Rejections Under 35 U.S.C. §102

Claims 1-20 are rejected under 35 U.S.C. §102 as allegedly anticipated by Price-Schiavi et al. Applicants have carefully reviewed the statement of the rejection as well as the cited document and respectfully traverse.

The rejection appears based on the view that the document reports a method of immunohistochemistry analysis of MUC4 expression in solid breast tumor samples obtained from patients with operable breast cancer. Assuming for the sake of argument only that this is being viewed as detecting expression of a receptor ligand in the samples, there is no detection of the receptor as featured in the claims. This deficiency alone is enough to indicate the absence of a *prima facie* case of anticipation.

Additionally, Applicants respectfully point out that the content of the cited document is contrary to the disclosure in the instant application. Specifically, the document appears to indicate that the presence of Muc4 inhibits the binding of ErbB2 to an anti-ErbB2 antibody. But a review of Example 1 and Table 1 in the instant application shows the discovery that expression of both HER2 (ErbB2) and MUC4 is correlated with effectiveness of trastuzumab (an anti-HER2 antibody). Indeed, the lack of MUC4 expression correlated with poor results in treatment with trastuzumab.

In light of the foregoing, Applicants respectfully submit that this rejection is misplaced and may be properly withdrawn.

Claim 12 was rejected under 35 U.S.C. §102 as allegedly anticipated by Price-Schiavi et al. because the kit does not recite ingredients or elements to distinguish the claim over the reference. Claim 12 has been revised to feature probes or antibodies that are not found in the cited document. Applicants respectfully submit that the revisions overcome the rejection. Reconsideration and withdrawal of the rejection thereof are respectfully requested.

Application Serial No.
10/599,550

Patent
20080-00008

The Commissioner is authorized to charge JHK Law's Deposit Account No. 502486 for any fees required under 37 CFR §§1.16 and 1.17 that are not covered, in whole or in part, by a credit card payment form submitted herewith and to credit any overpayment to said Deposit Account No. 502486.

Respectfully submitted,

JHK Law

Dated: December 11, 2007 By: Joseph Hyosuk Kim, Ph.D.
Registration No. 41,425

JHK Law
P.O. Box 1078
La Canada, CA 91012-1078
Telephone: (818) 249-8177
Facsimile: (818) 249-8277